

REMARKS

Claims 178-181 are pending in this application. Claim 178 and 179 are amended herein, and new claims 182 and 183 are added. Support for these amendments can be found throughout the specification. No new matter has been introduced.

In view of these amendments and the remarks that follow, Applicant submits that the application is now in condition for allowance and an early action to that effect is respectfully requested.

Priority

In the Office Action dated January 21, 2010 (hereinafter, "Office Action"), Applicant notes the Examiner's assertion that the pending claims are not supported by the disclosure of priority application no. 60/037,921, filed February 12, 1997, and will be afforded the filing date of the priority application no. 60/064,687, filed November 5, 1997. Without acquiescing with the Examiner's statements, Applicant notes that the prior art rejections are based on art published in 1993 and 1995, more than a year before either priority date, and thus the determination of priority for these claims has no bearing on the current prior art rejections.

Claim Rejections under 35 U.S.C. § 102(b) over Rigler

Claim 178 stands rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Rigler et al., J. Biotechnol. 41:177-186 (1995) (hereinafter, "Rigler"). See Office Action at pages 4-5 and 9-11. Applicant respectfully traverses and submits that Rigler does not anticipate claim 178 at least because it does not disclose, either expressly or inherently, at least two different elements of claim 178. First, Rigler does not disclose the use of a "tethered" polymerase as recited in pending claim 178. On the contrary, the polymerase used Rigler is apparently un-tethered, *i.e.*, free floating. See, *e.g.*, Rigler at 182, col. 2 to 183 and Figure 7. Second, Rigler does not disclose a method comprising detecting a signal from a unit specific marker of a nucleic acid molecule while the nucleic acid molecule is moved relative to electromagnetic radiation by a polymerase. For example, as discussed in Applicant's prior response, pages 182-183 and Figure 7 of Rigler disclose the autocorrelation function of M-13 DNA molecules labeled by incorporation of Rhodamine UTP using a primer and Klenow DNA polymerase. The signals

from the labeled nucleic acid molecules are *not* detected while the molecules are moved relative to electromagnetic radiation by the polymerase.

For at least these reasons, reconsideration and withdrawal of the rejection of claim 178 under 35 U.S.C. § 102(b) over Rigler is respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a) over Rigler in view of Vurek

Claim 180 stands rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Rigler in view of Vurek et al., U.S. Pat. No. 5,119,463, issued June 1992 (“Vurek”). See Office Action at pages 5-6. According to the Examiner, Rigler teaches all of the elements of claim 180 except for the use of a waveguide, and Vurek allegedly supplies this missing element because it discloses the use of a waveguide.

Applicant respectfully traverses and submits that the proposed combination of Rigler and Vurek, even if proper, does not render claim 180 obvious because this combination does not yield at least two different elements of claim 180. The teachings of Rigler are discussed above. At a minimum, Rigler does not teach or suggest the use of a tethered polymerase; nor does it teach or suggest a method comprising detecting a signal from a unit specific marker of a nucleic acid molecule while the nucleic acid molecule is moved relative to electromagnetic radiation by a polymerase. Vurek cannot provide either of the missing elements, because it does not teach or suggest the use of a tethered polymerase, nor does it teach detecting a signal from a unit specific marker while the nucleic acid molecule is moved relative to electromagnetic radiation by a polymerase.

When, as here, the proposed combination of references relied on to support a § 103 rejection does not teach or suggest each and every element of the claim, the burden is on the Examiner to articulate why the missing elements would have been obvious to the skilled artisan at the time the invention was made. If the Examiner fails to meet this threshold, then Applicant need not provide evidence of nonobviousness. See, e.g., MPEP § 2142. Here, the Examiner has not articulated any basis whereby the missing elements would have been obvious to the skilled artisan, and has therefore failed to establish a *prima facie* case of obviousness.

For at least these reasons, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 180 under 35 U.S.C. § 103(a) over Rigler in view of Vurek.

Claim Rejections under 35 U.S.C. § 102(b) over Higuchi

Claims 178 and 179 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Higuchi et al., Nature Biotech. 11:1026-1030 (1993) (“Higuchi”). According to the Examiner, Higuchi allegedly discloses all the elements of the rejected claims. *See* Office Action at pages 7-8. Applicant respectfully traverses and submits that Higuchi cannot anticipate claims 178 and 179 at least because it does not disclose, either expressly or inherently, at least two different elements of the rejected claims. First, Higuchi does not disclose the use of a tethered polymerase; instead, Higuchi teaches the use of Taq DNA polymerase that is un-tethered, i.e., free-floating, in the PCR reaction mixture. *See, e.g.*, Higuchi at 1030 (“Experimental Protocols” section). Second, Higuchi does not disclose a nucleic acid molecule labeled with a unit specific marker. *See, e.g.*, Specification as filed, page 73, lines 8-10 (“As used herein, a ‘unit specific marker’ is a compound which specifically interacts with one or more units of a polymer and is capable of identifying those units.”). Higuchi teaches the use of ethidium bromide (“EtBr”), a dye that *non-specifically* interacts with the nucleic acid molecule and moreover is *not* capable of identifying the unit to which it binds. Thus, Higuchi does not disclose use of a unit specific marker.

For at least these reasons, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 178 and 179 under 35 U.S.C. § 102(b) over Higuchi.

Claim Rejections under 35 U.S.C. § 103(a) over Higuchi in view of Vurek

Claims 180 and 181 stand rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Higuchi in view of Vurek. *See* Office Action at pages 8-9. According to the Examiner, Higuchi teaches all of the elements of claim 180 except for the use of a waveguide, and Vurek allegedly provides this missing element because it discloses the use of a waveguide.

Applicant respectfully traverses and submits that the proposed combination of Higuchi and Vurek, even if proper, does not render claims 180 and 181 obvious because this combination does not yield at least two different elements of the rejected claims, and the Examiner has failed to establish a *prima facie* case of obviousness for these missing elements. First, claims 180 and 181, which depend from claims 178 and 179 respectively, both require use of a tethered polymerase. Second, both claims require the use of a unit specific marker. The teachings of Higuchi are discussed above; at a minimum, neither Higuchi nor Vurek teaches or suggests the

use of a tethered polymerase, or a unit specific marker. Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has not articulated any reasoning whatsoever to support a finding that these missing elements would have been obvious to the skilled artisan.

For at least these reasons, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 180 and 181 under 35 U.S.C. § 103 as obvious over Higuchi in view of Vurek.

Rejection Under 35 U.S.C. § 112, Second Paragraph (indefiniteness)

Claims 178-181 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite based on their recitation of various terms. Applicant respectfully traverses.

First, the Examiner asserts that claims 178 and 180 are indefinite because they recite the limitation “by a polymerase”. Office Action at pages 6-7. According to the Examiner, there is insufficient antecedent basis for this limitation because “there is no mention or requirement in the claim for labeling with a polymerase.” Office Action at page 6. Without acquiescing in the basis for the Examiner’s rejection and solely in the interests of expediting prosecution, Applicant has amended claims 178 and 180 to recite detecting a signal while the nucleic acid is moved relative to electromagnetic radiation by a tethered polymerase, and submits that the pending claims fully satisfy the requirements of § 112, second paragraph because their meaning is readily ascertainable by the person of skill in the art. Applicant, however, strongly disagrees with the Examiner’s analysis, which can be read as suggesting that the claims require labeling with a polymerase. The Examiner’s characterization is erroneous and impermissibly imports limitations into the pending claims, which contain no such requirement. While embodiments comprising labeling with a polymerase are encompassed by the claims, the claims are not limited to such embodiments and should not be construed as such. Claims 178 and 180 only require detecting a signal from the unit specific marker “while the nucleic acid is moved relative to electromagnetic radiation by a tethered polymerase”, a requirement for which there is ample antecedent basis in the claims, and whose meaning is clear and definite under § 112.

Furthermore, even assuming that the limitation “by a tethered polymerase” lacks antecedent basis, the Examiner’s rejection is still improper because the meaning of this limitation is amply clear to the skilled artisan. As the Board of Appeals has repeatedly clarified, claim

terms that lack antecedent basis are not indefinite as long as the scope of the claim is “reasonably ascertainable” by one of skill in the art. *See, e.g., Ex Parte Rodriguez*, Appeal No. 2004-1331 (Bd. Pat. App. & Int. 2002) (reversing the Examiner’s indefiniteness rejection of a claim limitation based on alleged lack of antecedent basis) (“The failure to provide explicit antecedent basis for terms does not always render a claim indefinite. As stated above, if the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite.”); *Ex Parte Buhan*, Appeal No. 2008-3441 (Bd. Pat. App. & Int. 2002) (reversing the Examiner’s indefiniteness rejection of a claim limitation based on alleged lack of antecedent basis); *Ex parte Porter*, 25 U.S.P.Q.2d 1144, 1146 (Bd. Pat. App. & Int. 1992); *see also* MPEP § 2142 (citing *Energizer Holdings Inc. v. Int’l Trade Comm’n*, 435 F.3d 1366, 77 USPQ2d 1625 (Fed. Cir. 2006)) (“[T]he failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite.”).

Second, the Examiner has rejected claims 178-181 under 35 U.S.C. § 112, second paragraph as allegedly indefinite based on their recitation of “wherein the nucleic acid is moved relative to the electromagnetic radiation” (as recited in claim 178) or “moving a nucleic acid past electromagnetic radiation using a polymerase” (as recited in claim 179). Office Action at pages 6-7. According to the Examiner, these terms are vague because, while these terms could imply that the polymerase is held stationary and the nucleic acid is moved, the claims do not require that the polymerase is tethered to the apparatus or held in place in some way; clarification is requested. Applicant traverses and respectfully submits that the Examiner is impermissibly reading limitations into the claims that are not necessary to ensure clarity of meaning. For example, the meanings of the phrases “wherein the nucleic acid is moved relative to electromagnetic radiation” and “moving a nucleic acid past electromagnetic radiation using a polymerase” are amply clear to the skilled artisan in light of relevant disclosure throughout the specification, including, for example, at page 30, line 21 to page 38, line 19; page 46, line 16 to page 47, line 5; page 105, line 1 to page 10. Based on such disclosure, the meaning of these limitations is readily ascertainable by the skilled artisan.

Nevertheless, without acquiescing in the Examiner’s rejection and solely in the interests of expediting prosecution, Applicant has amended claims 178 and 179 (and as a result, all claims

depending therefrom) to recite the use of a “tethered” polymerase, thereby rendering this aspect of the Examiner’s rejection moot.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 178-181 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully requested.

CONCLUSION

In view of the amendments and remarks made herein, Applicant respectfully submits that the application is now in condition for allowance, and an early action to that effect is respectfully solicited. An interview with the Examiner to discuss the outstanding rejections is respectfully requested, and the Examiner is invited to contact the undersigned agent at the telephone number provided below.

Applicant hereby authorizes the Commissioner to charge any additional fees that may be required in connection with this application and/or to credit overpayment to **Deposit Account No. 50-3994**. In the event that additional fees or extensions of time are required, Applicant herein petitions for the necessary extension of time under 37 C.F.R. § 1.136(a) and authorizes the Commissioner to charge these fees or credit any overpayment associated with this or any other filing to this deposit account. This is not an authorization to pay the issue fee.

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